

Appln. No. 09/392,476  
Examiner: R.A. Wax  
Group Art Unit: 1653  
Confirmation No.: 1211

## REMARKS/ARGUMENTS

Claims 1, 4-29 and 32-33 remain pending in this application. Claims 8-21 and 26-29 have been amended, and claims 22 and 23 cancelled without prejudice or disclaimer.

### Rejection under 35 U.S.C. 112

Claims 8-21 and 26-29 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter.

In particular, the Examiner requested that the term "fungi" in claims 8-18 and 26-29 be replaced with --fungus--. Applicants have replaced the term "fungi" with the singular term --fungus-- in these claims.

The Examiner stated that the term "*Penicillum*" in claim 10 is improper and required its removal. Applicants note that that term has been amended to read *Penicillium* which is a filamentous fungus, and it is now correctly stated within claim 10.

Examiner also stated that the purification of the protein of interest is not part of the step of causing the fungi to produce. Applicants have amended claims 19-21 to remove the phrase "wherein the step of causing the fungi to produce [the protein of interest]" and to replace the term "comprises" with "comprising". Applicants submit that these claims are now directed to an additional step in the recited method. In light of the above amendments, withdrawal of the rejection of claims 8-21 and 26-29 under 35 U.S.C. 112 is respectfully requested.

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## **Rejection under 35 U.S.C. 102**

The Examiner has rejected claims 22 and 23 under 35 U.S.C. 102(b), alleging that the claims are anticipated by hemoglobin. The Examiner indicates that the claims are not limited to any particular protein, and thus hemoglobin produced by the claimed process would be identical to hemoglobin produced by any other process. Applicants respectfully disagree with the Examiner's rejection.

Applicants submit that claims 22 and 23 are directed to a protein produced by the process of claims 14 and 20, respectively. Claim 20 depends from claim 14, which is a method claim directed to the production of a protein of interest in a filamentous fungus, and includes the step of transforming the filamentous fungus with the nucleic acid sequence of claim 6. Claim 6 relates to a nucleotide sequence defined in claim 1, further comprising an intervening sequence. The nucleotide sequence of claim 1 clearly defines the gene of interest to encode a protein selected from the group consisting of a mannanase, a laccase, an endoglucanase, and a cellobiohydrolase. Thus, claims 22 and 23 are ultimately directed to a mannanase, a laccase, an endoglucanase and a cellobiohydrolase produced by the method of claims 14 and 20, respectively. As such, Applicants submit that hemoglobin does not anticipate the subject matter of these claims.

Nevertheless, Applicants have cancelled Claims 22 and 23 in order to render the rejection moot. As claims 22 and 23 have been cancelled, Applicants request the withdrawal of the Examiner's rejection of these claims under 35 U.S.C. 102.

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### Rejection under 35 U.S.C. 103

The Examiner has rejected claims 1, 4-29, 32 and 33 under 35 U.S.C. 103(a), alleging that the claims are unpatentable over International Publication No. WO 93/24621 (Suominen et al.) in view of U.S. Patent No. 5,591,619 (Xin-Liang et al.) Applicants respectfully traverse the Examiner's rejection.

Independent claims 1 and 13 are directed to a nucleotide sequence comprising a regulatory region selected from cbh1, cbh2, eg1, eg2, eg3, eg5, xln1, and xln2, in association with a xylanase secretion signal and a gene encoding a mannanase, a laccase, an endoglucanase or a cellobiohydrolase. Applicants submit that neither Suominen et al., Xin-Liang et al., or a combination of these two references teach or suggest nucleotide sequences to be used for the expression of a mannanase, laccase, endoglucanase or cellobiohydrolase.

In order for an invention to be "obvious" within the meaning of 35 U.S.C. 103 in view of a combination of references, the combination must be suggested in the prior art or by the very nature of the cited references. In re Geiger, 815 F.2d 686, 2 U.S.P.Q. 2d 1276 (Fed. Cir. 1987); Uniroyal Inc. v. Rudkin-Wiley Corp., 837 F.2d 1044, 5 U.S.P.Q. 2d 1434 (Fed. Cir. 1988); Interconnect Planning Corp. v. Feil et al., 774 F.2d 1132, 227 U.S.P.Q. 543 (Fed. Cir. 1985). The mere fact that a prior device or construct can be modified to produce the claimed invention is not a proper basis for an obviousness rejection unless the art suggests the desirability of such a modification. In re Gordon et al., 733 F.2d 900, 221 U.S.P.Q. 1125 (Fed. Cir. 1984). A showing that two or more references are related to a similar subject matter does not, by itself, suggest the

possibility of desirability of a combination of those references. In re Levitt, 11 U.S.P.Q. 2d 1315 (Fed. Cir. 1989) (unpublished).

Suominen et al. teaches an expression construct comprising a cbh1 promoter with a xylanase 2 (Example 2; page 51, lines 9-13) or xylanase1 (Example 4; page 61, lines 10-13) secretion signal in combination with their native coding sequence, either xylanase 2 or 1, respectively. There is no teaching or suggestion that the xln1 or xln2 coding region within this construct may be replaced with another gene encoding a desired enzyme. Suominen et al. suggests that the coding sequence should retain its own signal sequence, except under certain circumstances; for example, if a desired protein does not possess its own signal sequence, or the signal sequence does not function well in *Trichoderma*, then the coding sequence may be operably linked to a signal sequence homologous or heterologous to *Trichoderma* (page 26, lines 12-17). However, no specific examples of a desired signal sequence, nor any evidence of the benefit of a specific signal sequence, is provided. Furthermore, there is no suggestion to produce a mannanase, laccase, endoglucanase or cellobiohydrolase using the specified nucleotide sequences.

Xin-Liang et al. disclose an *A. pullulans* xylanase (APX-II or xynA) and secretion signal. The document states that the secretion signal may be used to increase the yield of foreign genes in host cells (column 8, lines 30-32) including filamentous fungi (col 8, lines 43-45), but preferably *Aurobasidium*, *S. cerevisiae* and other yeasts (col 8, lines 33-36). According to Xin-Liang et al., the APX-II signal sequence in combination with a foreign gene expressible in *S. cerevisiae* may be inserted into a vector under control of a promoter expressible in the host (column 8, lines 63-66), preferably a constitutive promoter such as

yeast enolase or yeast alcohol dehydrogenase (column 9, lines 2-3 and 8). Xin-Liang et al. states that the signal peptide can be fused to other proteins for secretion of high levels of recombinant proteins from *S. cerevisiae* (column 11, lines 32-34).

However, there is no suggestion or specific teaching in Xin-Liang et al. of the combination of regulatory regions, secretion signal, and gene of interest as claimed in the present application. In fact, the preferred embodiments disclosed in Xin-Liang et al. (see above) are quite different than those presently contemplated. In Example 6 of Xin-Liang et al., the APX-II signal sequence and xylanase gene are in operative association with a gal1 promoter, which is clearly not within the scope of claim 1. There is no explicit instruction in Xin-Liang et al. to produce a nucleotide sequence comprising a regulatory region selected from *cbh1*, *cbh2*, *eg1*, *eg2*, *eg3*, *eg5*, *xln1*, and *xln2*, in association with a xylanase secretion signal and a gene encoding a mannanase, a laccase, an endoglucanase or a cellobiohydrolase. Furthermore, there is no support in the prior art document that the APX-II/xynA secretion signal is capable of increasing the yield of any protein other than xylanase in combination with a gal1 promoter, in any host other than *S. cerevisiae*.

Applicants submit that a person of skill in the art would not have been led clearly and directly to the presently claimed invention given the disclosures of Suominen et al. and Xin-Liang et al., alone or in combination.

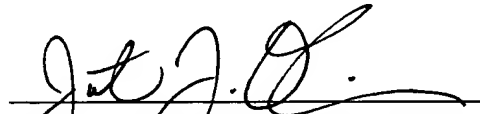
For the above reasons, Applicants submit that the invention as presently claimed is not obvious in view of Suominen et al. and Xin-Liang et al. Applicants respectfully request the withdrawal of Examiner's rejection to claims 1, 4-29, and 32-33 under 35 U.S.C. 103.

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It is respectfully submitted that the above-identified application is now in a condition for allowance and favorable reconsideration and prompt allowance of these claims are respectfully requested. Should the Examiner believe that anything further is desirable in order to place the application in better condition for allowance, the Examiner is invited to contact the applicants' undersigned attorney at the telephone number listed below.

Respectfully submitted

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Attachments: Eleven (11) Sheets of Replacement Drawings

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### **Drawings**

Attached are formal drawing sheets to be substituted for the corresponding informal drawing sheets on file. No new matter has been added in the new sheets.